ACCESS TO UNLICENSED MEDICINES

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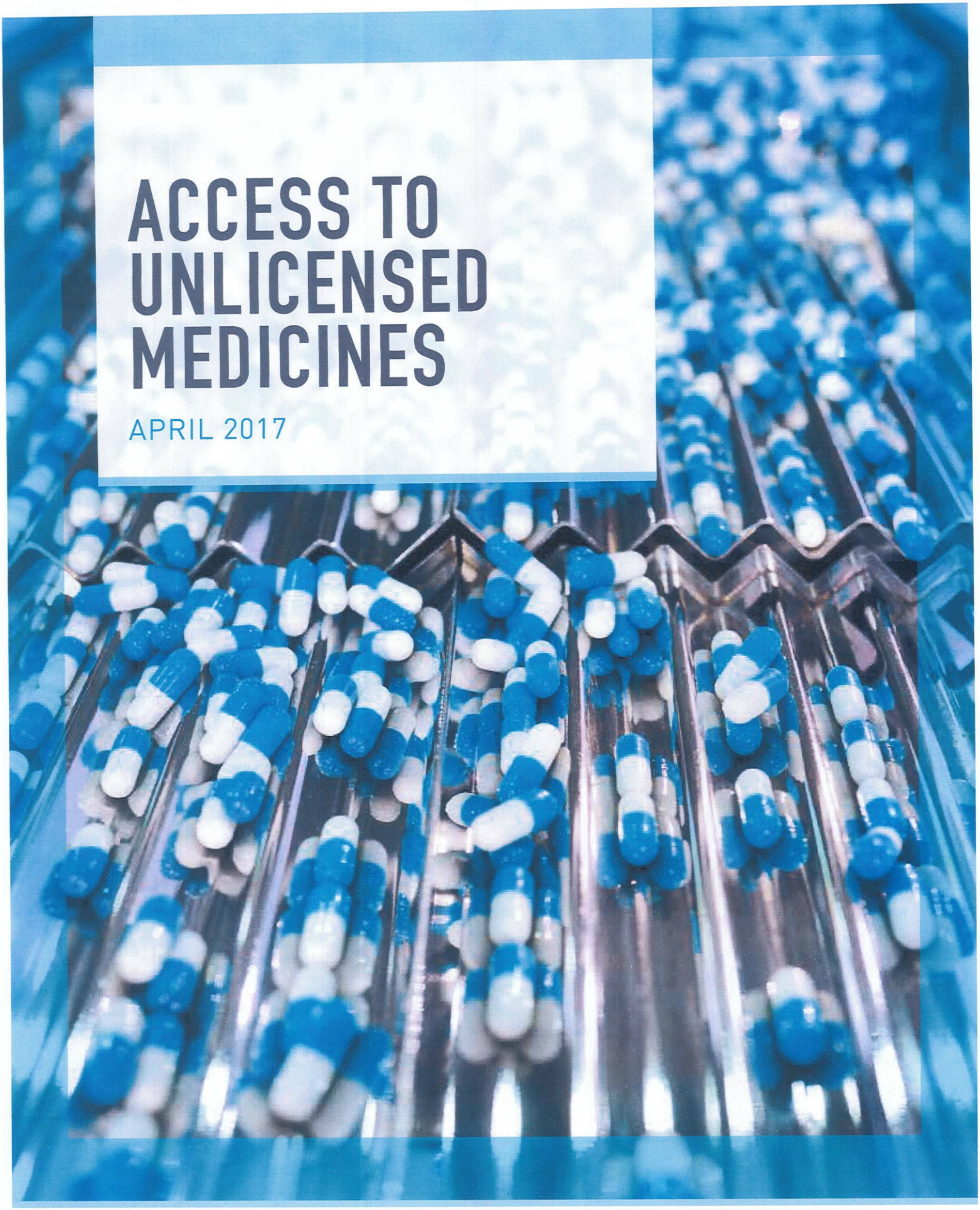

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European Lawyers' Conference on Pharmaceutical and Health Care Affairs

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A. General

1. Are doctors entitled to write prescriptions for unlicensed products (whether under national health schemes or on a private supply basis) and, if so, are there any restrictions on them doing so?

Yes, doctors are entitled to write prescriptions for unlicensed products. Note, however, that unlicensed products can be administered and reimbursed by the social insurance[1] only in exceptional cases and according to the reports in the international literature and documented on an individual basis, upon a substantiated request of the social insurance agencies. Medicinal products introduced with urgent procedures with the approval of the National Organization for Medicines ('EOF') are reimbursed by the social insurance agencies, regardless of whether they are included in the Positive List.

2. Do national rules exist in your jurisdiction allowing the manufacture and supply of unlicensed medicines on a "named patient" or "compassionate use" basis and, if so, what legislation implements them and has guidance been issued by the competent authorities on their interpretation?

Yes. Article 2 of ministerial decision (MD) 85037/10/2011 (Government Gazette (GG) B' 558/08.04.2011) (the 'Ministerial Decision') provides for early access to pharmaceutical products in groups of patients and/or individuals. In particular, 'Personal license for early access to the medicinal product' (the Named Patient Program, 'NPP') applies under the terms and conditions described in the abovementioned ministerial decision, i.e. in specifically justified cases, for a specific patient, upon the request of the treating doctor and under his/her exclusive and unlimited liability, if it is concluded, based on the available data, that the ratio benefit/risk is positive in favor of the anticipated benefit.

In addition to the above, the same legislation also provides for 'group scheme for early access to the medicinal product' (the 'Group Scheme'). This scheme applies upon the license of EOF, for a specific group or subgroup of patients who are included in a general group treatment and follow-up scheme. This scheme is based on the analytical criteria that are included in an approved therapeutic protocol for the administration of an 'early-access' medicinal product, if it is concluded that the ratio benefit/risk is positive in favor of the anticipated benefit.

3. Are the requirements different for establishment of a compassionate use scheme for groups of patients while an application for MA is pending, as opposed to where supply is for a particular patient and is made at the request of that patient's HCP?

No differentiation applies.

4. Are there any special rules applicable to hospitals and community pharmacists preparing 'custom made' products for individual patients? How has the decision of the ECJ in Case 535/11 Novartis Pharma GmbH v Apozyt GmbH been implemented in your jurisdiction?

Yes. In article 7 of presidential decree (PD) 312/1992, (GG 157/A/16.9.1992), there is a provision concerning the manufacture of custom made medicinal products by the pharmacists. In addition, pursuant to MD 3294/2011 (GG B' 2456/3-11-2011), as amended, 'custom made' preparations are reimbursed with a prescription in accordance with the relevant diagnosis. The decision of the ECJ in Case 535/11 Novartis Pharma GmbH v Apozyt GmbH is respected and the relevant provisions of art. 5 of the EU Directive 83/2001, as in force, is incorporated as in article 4 of the Greek MD 32221/2013, which transposed this Directive (EC) No 83/2001 into the Greek legal system.

5. Advanced therapy medicinal products are excluded from the scope of the authorisation requirements of the Directive in certain circumstances set out in Regulation (EC) No 1394/2007, such as where manufactured on a small scale 'custom made' basis and used in hospital. Where such exclusions apply, how has national law in your jurisdiction provided for these exceptions and are there material differences in the approach adopted compared with use of other types of unlicensed medicinal products?

Pursuant to MD 32221/2013 (GG B' 1049/2013), transposing Directive (EC) No 83/2001 as amended by Regulation (EC) No 1394/2007, advanced therapy medicinal products ('ATMP's'), as defined in EU Regulation No 1394/2007, which are systematically produced, according to specific qualitative criteria and used in Greece in a hospital under the exclusive professional liability of a doctor, in order to correspond to a personalized medical prescription for a single patient, fall outside the scope of the MD.

1. E.O.P.Y.Y. is the main social insurance agency in Greece.

This means that no MA is required for ATMPs where they meet the above mentioned exception. In the case of unlicensed medicinal products either there is an application for a MA pending or they are still at clinical trial phase. Of course, both in the case of an ATMP and the NPP process and Group Scheme, it is upon the treating doctor to prove the patient's need to take the specific medicinal product, even if in terms of prescription the approach is differentiated.

B. Conditions

6. What are the basic conditions that must be met for a company to supply an unlicensed medicine?

The supply of unlicensed products is not restricted to particular therapeutic areas of serious and/or life threatening disease as well as to particular types of medicinal products.

The doctor is entitled to request approval for supply of an unlicensed product and, upon approval, the process for the import and supply of the requested product is run by the pharmacist involved.

It is upon the treating doctor to decide on a patient need basis which is the best treatment for a patient. So, it is sufficient that a doctor decides that an authorised product or its particular strength, which is available or its particular excipients does not meet the patient's special clinical need. However the doctor will have to accompany and support the specific request for an unlicensed product with a medical opinion, justifying why the authorised product for the clinical need in question (if any) is not appropriate from a medical perspective.

Decision C-185/2010 is respected in Greece. Further to this, to the opinion of the Greek Council of State (Decision 1749/2016), "under Article 21 paragraph 2 of the Constitution (social right to health: the State is obliged to provide for the health of citizens), the quality and appropriateness of pharmaceutical care is a prominent criterion, among other criteria, for addressing the needs of each patient in an appropriate and personalised manner."

Treatment has to be decided and administered in accordance with the standards of medical science by the physician who is directly responsible for the patient; in so doing, the physician must not be subject to unreasonable restrictions on the exercise of his/her tasks and the choice of the appropriate medication. At this point it has to be taken in consideration that for an unlicensed product to be imported in Greece, this must be authorized somewhere, either in EU or in a third country.

C. Procedural requirements

7. What are the procedural/administrative requirements relating to a supply that is legal under national rules?

The rules relating to supply of unlicensed products are the same for these products either manufactured locally, within EU or outside EU. In any case, an approval is required from EOF, before an unlicensed product is imported or prepared and supplied to a patient. Such approvals apply either for particular patients (individuals) or for specific group of patients, as described in our answer for question 2. The approval is valid for maximum one year and it can be renewed, provided that the approval's conditions are still applicable. The early access license is terminated as soon as the drug in scope is approved by the competent authorities. From this day onwards, the supply thereof is subject to the regular supply's terms. The early access license is also terminated in case the application for the granting of a market authorisation is rejected on substantial grounds.

According to local legislation, for the import of an unlicensed product, details of the patient as well as the patient's consent are required. Such consent can be given by the patient's legal representative, in case of the patient's impediment. Moreover, a confirmation on the special need is needed directly from the patient's/ patients' doctor, who is responsible for the administration of the imported unlicensed product.

The supplier must keep on file a statement/evidence from the doctor/pharmacist requesting an unlicensed product to meet a special clinical need.

In addition to the above, in case of early access to medicinal products (whether under national health schemes or on a private supply basis), the responsible doctor must keep records relating to the supply of the unlicensed products for a period of 15 years.

Moreover a publically available official list, created and kept by the competent authority, EOF, makes reference to unlicensed products under the early access programs.

With respect to the notification of adverse events or other new information relevant to safety of unlicensed medicinal products, standard pharmacovigilance requirements for manufacturers or importers apply.

D. Labelling and product information

8. What are the requirements (if any) for labelling of the product and for patient or HCP product information in respect of the unlicensed product that is supplied?

No specific labelling requirements apply.

9. What, if any, guidance has been given on the product liability exposure of HCPs or suppliers in respect of the prescription and supply of the unlicensed product? Are there any special compensation rules or guidelines for patients injured by unlicensed products?

There is civil and criminal liability of HCPs and/ or suppliers with respect to the supply of unlicensed products (whether under national health systems or on a private supply basis), as provided for by the respective Greek legislation.

E. Advertising

10. To what extent can a company make known or "advertise" its ability to meet requests for unlicensed products? How has the decision of the ECJ in Case C-143/06 Ludwigs - Apotheke relating to price lists for unlicensed products been interpreted in your jurisdiction? What is the limit for the contents of such a list before the list is treated as "promotional".

Any price list for unlicensed products will be considered as promotional material, therefore it is prohibited since advertising of unlicensed products is not permitted according to local laws and regulations (MD 85037/2011 (GG 1049/ B/2011)). The decision taken by the ECJ in Case C-143/06 Ludwigs - Apotheke has not been interpreted in any way in our jurisdiction.

11. Are the rules different for making known the availability of compassionate use/early access schemes?

Such information must come through doctors, who may inform their patients of the existence of such schemes.

12. Are the rules relaxed where an MA is surrendered on commercial grounds, but the company agrees to meet requests for the now unlicensed product for patients already controlled on that product?

The rules are not relaxed in this case.

F. Financial aspects

13. Are suppliers of unlicensed products (outside the clinical trial setting) entitled to charge for supply of such products?

Yes. Standard rules apply.

14. Is the cost of an unlicensed product reimbursed under national health schemes and, if so, are there any restrictions?

If in the context of an NPP or a Group Scheme for early access, medicinal products introduced with urgent procedures with the approval of EOF are reimbursed by the insurance agencies, regardless of whether they are included in the Positive List.

15. Are doctors subject to any professional rules/published standards relating to the prescription of unlicensed products such as when it is legitimate to prescribe unlicensed products and what special responsibilities arise in relation to consent from patients and liability for any injury arising?

Please see our answers to questions 1 and 5.

G. Other matters

16. Are there any special rules or guidance notes applicable to supply of unlicensed products to clinical trial patients after the end of a trial at a centre in your country? Do ethics committees seek to control the terms for continued access or termination of treatment at the end of the trial? Are there any special requirements relating to compensation for injury.

Rules applicable to supply of unlicensed products in clinical trials are provided by MD 59676/2016 (GG / B/ 4131/22.12.2016), with which EU Regulation 536/2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC has been transposed into the Greek legal system.

In Greece products can be supplied to trial patients even after a trial has been completed. Once the trial has been completed a new protocol will be created to manage that scenario.

Pursuant to Annex I of this EU Regulation, the protocol of the clinical trial needs to include, among other topics, a description of the arrangements for taking care of the subjects after their participation in the clinical trial has ended, where such additional care is necessary because of the subjects' participation in the clinical trial and where it differs from that normally expected for the medical condition in question.

17. Have the authorities in your country developed any country specific "early access" schemes allowing for the supply of unlicensed medicinal products before they gain a marketing authorisation and, if so, what are the main features of the scheme?

The 'early access' schemes that apply for unlicensed medicinal products are the ones provided for by the Ministerial Decision, as above described. Please see also our answer to question 2.

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